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EDITORIAL COMMENT

Paravalvular Regurgitation After TAVR

A Doppler Dilemma*

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Paravalvular aortic regurgitation (PVR) following transcatheter aortic valve replacement (TAVR) remains the Achilles heel of this technology. In large clinical trials that included an echocardiographic core laboratory, the incidence of significant (moderate or severe) PVR after TAVR has been reported to be between 4% and 12% (1-5). This 3-fold variation in the reported incidence of significant PVR reflects the current challenge faced by many TAVR teams: how to identify and quantify significant PVR after TAVR. Many factors contribute to the varied reports of PVR incidence, including: 1) the study of either balloon expandable or self-expanding transcatheter heart valves; 2) the timing of the echocardiographic assessment (intraprocedural, hospital discharge, or 12-month follow-up); and 3) the specific measures performed by each echo core laboratory using differing expert guidelines (6) or consortium protocols (7) to quantify PVR severity. The impact of PVR on patient mortality has also been challenging to define. The clinical trial data has suggested that a significant mortality hazard exists across a wide spectrum of PVR severity. Increased mortality has been reported with mild PVR (3) and moderate or severe PVR (4).

Why is PVR so difficult to quantify? Several elements come into play, including: patient-specific aortic annular and/or leaflet geometry and calcium distribution that contribute to incomplete apposition of the transcatheter heart valve to the annulus; the paravalvular regurgitant jet may be single or multiple; the regurgitant jets are often crescentic and eccentric with an axis of flow that may not be well visualized from any standard Doppler imaging window; the interface of prosthetic material against heavily calcified tissues can create imaging artifact or dropout; and the lack of a clear reference standard to consistently define PVR severity, which is one of the biggest challenges. Despite the clear need to develop robust and reproducible methods to identify PVR after TAVR, the task remains difficult, and the "best" parameter has yet to be defined.

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In this issue of *iJACC*, Mihara et al. (8) present a clinical experience that may provide some guidance in this regard. They report on a large (N = 390) single-center experience that used intraprocedural transesophageal echocardiography (TEE) to assess PVR immediately following balloon-expandable TAVR. They defined the presence of significant PVR based on evaluation of the short axis of the vena contracta area (VCA) of the regurgitant jet. In keeping with both the Valve Academic Research Consortium-2 (VARC-2) and American Society of Echocardiography (ASE) guidelines (6,7), PVR was mild if the VCA was $\leq$9 mm^2, moderate if the VCA was 10 to 29 mm^2, and severe if the VCA was $\geq$30 mm^2. Moderate or severe PVR were both considered to represent a significant lesion and thus were pooled to define significant PVR in any patient with a VCA of $\geq$10 mm^2. In a retrospective fashion, and using several different subsets of the total study population, they used various spectral and color Doppler measures to describe post-procedural aortic regurgitation (PAR) severity as either nonsignificant or significant, based on the VCA reference standard. In addition to exploring several of the short-axis color Doppler jet features, including circumferential jet extent, they also reported on the evident association between PAR severity and: 1) the extent of the color Doppler jet within the left ventricular outflow tract (LVOT); and 2) the holodiastolic flow reversal in the proximal descending aorta.

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HOLODIASTOLIC FLOW REVERSAL

From the total study cohort of 380 patients, pulse-waved Doppler of the descending aorta was attempted in 128 patients. Within that subgroup of tested patients, the recognition of consistent holodiastolic flow reversal was reported to have modest sensitivity and impressive specificity (58% and 100%, respectively) for the detection of significant PVR. In addition, the finding of persistent holodiastolic flow reversal was reported to be significant both in univariable and multivariable logistic regression analyses for identifying significant PVR. Taken together, these results suggest that the classic Doppler finding of flow reversal within the proximal descending aorta is a powerful indicator of the presence of significant PVR. However, a note of caution is required. In this retrospective study, only one-third of the total population had Doppler interrogation of the descending aorta performed. Because the descending aortic Doppler study was not performed in all patients, it is reasonable to surmise that it was done only in those situations when significant PVR was suspected based on a collection of other imaging features. If so, then this Doppler study selection bias could heavily influence the apparent excellent performance of this classic Doppler measurement. Important previous work by Tribouilloy et al. (9) published 24 years ago reported better sensitivity and similar specificity (88.5% and 96.0%, respectively). Their patient population was substantially younger and had chronic native aortic valve regurgitation, but their study nevertheless established that diastolic flow reversal is strongly associated with significant aortic regurgitation (AR). Later studies compared the presence of diastolic flow reversal against a reference standard of color Doppler flow convergence and reported rather poor sensitivity but good specificity (45% and 87%, respectively) for AR quantification (10). Mihara et al. (8) report a similar performance for Doppler flow reversal despite applying this measurement in a peri-procedural TAVR population with acute PAR. Thus, the test performance is perhaps better than expected because Doppler measures of aortic flow may be affected by heart rate, left ventricular compliance, the transvalvular gradient, and age-related changes in vascular compliance. The study by Mihara et al. (8) represents an important effort to associate holodiastolic flow reversal and significant PVR after TAVR with compelling specificity.

REGURGITANT JET EXTENT

Mihara et al. (8) also reported that the extent of the color Doppler jet length was another independent predictor of the presence of significant PVR. A regurgitant jet that extended within the LVOT past the level of the anterior mitral leaflet was a strong predictor of significant PVR in multivariable analysis. This color Doppler measurement is a variation on an old parameter that has largely been exiled from current echocardiography practice guidelines that specifically recommend against its use as a sole criterion for the quantification of AR severity (6). This guideline recommendation is largely based on a single study by Perry et al. (11), which compared a mosaic of color Doppler within the LVOT against an angiographic reference standard of AR severity. In that study, there was no significant correlation between native AR jet length and the angiographic assessment of AR severity.

Therefore, is there something unique about PAR after TAVR that predicts that the performance of this color Doppler measurement should improve? Several features of PVR jets would predict that measurement of jet extent would perform less well, not better, after TAVR. Color Doppler is a map of velocities and not flow, so it is well recognized that flow momentum (influenced by the pressure gradient) can affect the size (and length) of a color Doppler jet independent of any change in the regurgitant volume. PAR also tends to be an LVOT “wall-hugging” jet, and this fluid-structure interaction may diminish the jet length, but not the regurgitant volume. In the study by Mihara et al. (8), 80% of all patients with some PVR had jet extent within the LVOT categorized relative to the anterior mitral leaflet (grades 1, 2, or 3). The correlation between jet extent grade and the VCA reference of significant PVR was positive ($r = 0.64$); however, the correlation between jet length and holodiastolic flow reversal was less impressive ($r = 0.38$). Nonetheless, these investigators concluded that both holodiastolic flow reversal and PVR jet extent are important predictors of significant PVR after TAVR.

VENA CONTRACTA AREA

Mihara et al. (8) reported using 2-dimensional (2D) TEE to assess the VCA, and define significant PVR as an area $\geq$10 mm^2. Limitations and technical considerations for VCA measurement have been described in detail (12), and neither the ASE guidelines nor the VARC-2 documents suggest that the PVR severity be quantified based on VCA measurement alone. Despite these concerns, Mihara et al. (8) reported that significant PVR defined by 2D VCA measurement was associated with a survival disadvantage. Although the duration of clinical follow-up differed considerably between the patient groups with and without PVR, survival data were available for all patients and indicated that significant PVR was associated with increased late mortality (hazard ratio: 2.4).

In the end, the study reported by Mihara et al. (8) is intriguing for its emphasis on holodiastolic flow reversal and perhaps resurrection of the concept of jet length within the LVOT as potentially important markers of significant PVR. Limitations to the impact of this study include the retrospective analysis of Doppler method subgroups and the single reference standard of VCA to define PVR severity. Nevertheless, a prospective TEE protocol with the systematic use of these and other measurements compared with important clinical outcomes will likely be how we decide which are the most valued echo parameters moving forward. Until then, the quantification of PVR remains an ongoing Doppler dilemma.

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